CLAIMS

What is claimed is:

1. A method for separating a molecular species of interest from a feedstream, comprising:

(a) filtering said feedstream by a tangential-flow filtration process through a filtration membrane having a pore size that separates said molecular species of interest from said feedstream, while maintaining flux at a level ranging from about 5 to 100% of transition point flux in the pressure-dependent region of the flux versus TMP curve, wherein transmembrane pressure is held substantially constant along the membrane at a level no greater than the transmembrane pressure at the transition point of the filtration, whereby said molecular species of interest is selectively separated from said feedstream such that said molecular species of interest retains its biological activity;

(b) filtering said feedstream by a microfiltration process; and

wherein said molecular species of interest is a protein.

2. The method of claim 1, further comprising fractionating said feedstream.

3. The method of claim 1, further comprising clarifying said feedstream.

4. The method of claim 1, further comprising diafiltering said feedstream.

5. The method of claim 1, further comprising concentrating said feedstream.

6. The method of claim 1, wherein the species of interest has a molecular weight of about 1 to 1000 kDa.

7. The method of claim 1, wherein all filtration stages are ultrafiltrations.

8. The method of claim 1, wherein said feedstream is milk.

9. The method of claim 1, wherein said feedstream is a cell lysate solution.

10. The method of claim 1, wherein said protein is a biopharmaceutical.

11. The method of claim 8, wherein the condition of said milk is selected from one of the following states:
    a) raw;
    b) diluted;
    c) treated with a buffer solution;
    d) chemically treated; and
    e) partially evaporated.

12. The method of claim 2, wherein said fractionation step utilizes ceramic filtration membranes.

13. The method of claim 3, wherein said clarification step utilizes ceramic filtration membranes.

14. The method of claim 2, wherein said fractionation step utilizes polymeric filtration membranes.

15. The method of claim 3, wherein said clarification step utilizes polymeric filtration membranes.

16. The method of claim 2, wherein said fractionation step utilizes cellulose filtration membranes.

17. The method of claim 3, wherein said clarification step utilizes cellulose filtration membranes.

18. The method of claim 2, further comprising optimizing systematic parameters.

19. The method of claim 18, wherein said systematic parameters include temperature, feedstream flow velocity, transmembrane pressure, feedstream concentration and diafiltration volume.

20. The method of claim 3, further comprising optimizing systematic parameters.

21. The method of claim 20, wherein said systematic parameters include temperature, feedstream flow velocity, transmembrane pressure, feedstream concentration and diafiltration volume.

22. The method of claim 1 wherein said molecular species of interest are biological entities selected from the group consisting of proteins, immunoglobulins, polypeptides, peptides, glycoproteins, RNA and DNA.

23. The method of claim 19, wherein the optimal temperature range is from 15 °C to 50°C.

24. The method of claim 19, wherein the optimal temperature range is from 20 °C to 35°C.

25. The method of claim 19, wherein the optimal temperature range is from 25 °C to 29°C.

26. The method of claim 21, wherein the optimal temperature range is from 15 °C to 50°C.

27. The method of claim 21, wherein the optimal temperature range is from 20 °C to 35°C.

28. The method of claim 21, wherein the optimal temperature range is from 25 °C to 29°C.

29. The method of claim 19, wherein the feedstream flow velocity is from 10 cm/sec to 100 cm/sec.

30. The method of claim 19, wherein the feedstream flow velocity is from 20 cm/sec to 60 cm/sec.

31. The method of claim 19, wherein the feedstream flow velocity is from 25 cm/sec to 45 cm/sec.

32. The method of claim 21, wherein the feedstream flow velocity is from 10 cm/sec to 100 cm/sec.

33. The method of claim 21, wherein the feedstream flow velocity is from 20 cm/sec to 60 cm/sec.

34. The method of claim 21, wherein the feedstream flow velocity is from 25 cm/sec to 45 cm/sec.

35. The method of claim 19, wherein the transmembrane pressure ranges from 2 psi to 40 psi.

36. The method of claim 19, wherein the transmembrane pressure ranges from 5 psi to 30 psi.

37. The method of claim 19, wherein the transmembrane pressure ranges from 10 psi to 20 psi.

38. The method of claim 21, wherein the transmembrane pressure ranges from 2 psi to 40 psi.

39. The method of claim 21, wherein the transmembrane pressure ranges from 5 psi to 30 psi.

40. The method of claim 21, wherein the transmembrane pressure ranges from 10 psi to 20 psi.

41. The method of claim 19, wherein the feedstream concentration is from 0.25X to 4X natural milk.

42. The method of claim 19, wherein the feedstream concentration is from 0.5X to 3X natural milk.

43. The method of claim 19, wherein the feedstream concentration is from 1.0X to 2X natural milk.

44. The method of claim 21, wherein the feedstream concentration is from 0.25X to 4X natural milk.

45. The method of claim 21, wherein the feedstream concentration is from 0.5X to 3X natural milk.

46. The method of claim 21, wherein the feedstream concentration is from 1.0X to 2X natural milk.

47. The method of claim 19, wherein the diafiltration volume range is from 1X to 20X the volume of concentrated MF retentate.

48. The method of claim 19, wherein the diafiltration volume range is from 3X to 15X the volume of concentrated MF retentate.

49. The method of claim 19, wherein the diafiltration volume range is from 5X to 10X the volume of concentrated MF retentate.

50. The method of claim 21, wherein the diafiltration volume range is from 1X to 20X the volume of concentrated MF retentate.

51. The method of claim 21, wherein the diafiltration volume range is from 3X to 15X the volume of concentrated MF retentate.

52. The method of claim 21, wherein the diafiltration volume range is from 5X to 10X the volume of concentrated MF retentate.

53. The method of claim 2, wherein ultrafiltration membranes are used for all filtering steps.

54. The method of claim 5, wherein ultrafiltration membranes are used for all filtering steps.

55. The method of claim 8, wherein said milk is treated with a solution selected from the group consisting of:

a) water;

b) a buffered aqueous salt solution;

c) chelating agent;

d) acid solution; and

e) alkali solution.

56. The method of claim 4, wherein said diafiltration utilizes ultrafiltration permeate.

57. The method of claim 4, wherein said diafiltration utilizes water.

58. The method of claim 4, wherein said diafiltration utilizes a buffered salt solution.

59. The method of claim 1, wherein the membranes used are cleaned with solutions of a temperature greater than 20°C.

60. The method of claim 1, wherein the membranes used are cleaned with solutions ranging in temperature from 20°C to 70°C.

61. The method of claim 1, wherein the membranes used are cleaned with solutions ranging in temperature from 40°C to 60°C.

62. The method of claim 1, wherein the membranes used are cleaned with an acid solution.

63. The method of claim 1, wherein the membranes used are cleaned with an alkali solution.

64. The method of claim 1, wherein the membranes used are cleaned with a hypochlorite solution.

65. The method of claim 62, 63 or 64, further comprising a water rinse following the use of the selected solution.

66. The method of claim 1, wherein the membranes used are sanitized prior to use with a hydroxide solution.

67. The method of claim 1, wherein the membranes used are sanitized prior to use with an alcohol solution.

68. The method of claim 1, wherein the membranes used are sanitized prior to use with a hypochlorite solution.

69. The method of claim 1, wherein the membranes used are cleaned for a period of from 20 minutes to 45 minutes.

70. The method of claim 1, further comprising filtering the filtrate from the filtration in a second tangential-flow filtration stage through a membrane having a smaller pore size than the membrane used in the first filtration stage, and recycling the filtrate of this second filtration stages back to the first filtration stage, whereby the process is repeated.